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EXAMINER

COLEMAN, BRENDA LIBBY

ART UNIT	PAPER NUMBER
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1624

DATE MAILED: 08/27/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/934,531

Applicant(s)

NIELSEN ET AL.

Examiner

Brenda Coleman

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 October 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 17-25 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 17-25 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Claims 17-25 are pending in the application.

This action is in response to applicants' amendment filed October 1, 2003.

Claims 1-8 and 12-16 were canceled and claims 17-25 are newly added.

Note: The applicants' are advised that this action is based on the use of PCT/DK00/00202 for the specification and the claims as originally filed.

Response to Arguments

Applicants' arguments filed October 1, 2003 have been fully considered with the following effect:

1. The applicants' amendments and remarks are sufficient to overcome the improper Markush rejection of claims 1-8 and 12-14 labeled paragraph 2) in the last office action, which is hereby **withdrawn**.
2. With regards to the 35 U.S.C. § 112, first paragraph rejection of claims 1-5, 7, 8 and 12-14, labeled paragraphs 4) and 6) in the last office action. The applicants' remarks concerning claim 1 such that the scope has been reduced; claim 12 is drawn to a method of using a relatively narrow group of nAChR modulators by amendment to claim 1 and claim 14 is drawn to the use of the nAChR modulators to treat four specified conditions. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims where the disorder is treatable with a nicotinic acetylcholine receptor ligand. As stated in the last office action it is difficult to treat many of the disorders claimed herein. Recent studies on experimental and clinical pharmacology of

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nicotinic acetylcholine receptors cited in Annual Reports in Medicinal Chemistry indicate that the following disorders may be associated with nicotinic acetylcholine receptors: senile dementia of the Alzheimer's type, Parkinson's disease, Huntington's chorea, tardive dyskinesia, hyperkinesia, mania, depression, attention deficit disorder, anxiety, dyslexia, schizophrenia, Tourette's syndrome and smoking cessation. The "nicotinic" effect with respect to Alzheimer's is hypothesized. Parkinson's Disease is "presently of unknown etiology" and recent studies have exhibited dosing problems as well as "unusually high placebo effects". The pathophysiology of Tourette's syndrome is unknown. The treatment of ulcerative colitis is currently "limited to anti-inflammatories, immunosuppressants and antibiotics". Additionally, there are other pathological non-CNS conditions, such as pouchitis and influenza virus-induced pneumonitis, where nicotine efficacy has been reported, but remains to be confirmed.

It is difficult to treat many of the disorders claimed herein. Instant claim language embraces disorders not only for treatment but for the prevention or prophylactics, which is not remotely enabled. It is presumed in the prevention of the diseases and/or disorders claimed herein there is a way of identifying those people who may develop osteoporosis, etc. There is no evidence of record, which would enable the skilled artisan in the identification of the people who have the potential of becoming afflicted with the disorders claimed herein.

Where the utility is unusual or difficult to treat or speculative, the examiner has authority to require evidence that tests relied upon are reasonably predictive of in vivo

efficacy by those skilled in the art. See *In re Ruskin*, 148 USPQ 221; *Ex parte Jovanovics*, 211 USPQ 907; MPEP 2164.05(a).

Patent Protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. Tossing out the mere germ of an idea does not constitute enabling disclosure. *Genentech Inc. v. Novo Nordisk* 42 USPQ2d 1001.

Newly added claims 23-25 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for reasons of record and stated above.

3. The applicant's amendments and arguments are sufficient to overcome the 35 USC § 112, first paragraph rejection of claims 8 and 12-14, labeled paragraph 5) of the last office action, which is hereby **withdrawn**.

4. The applicant's amendments and arguments are sufficient to overcome the 35 U.S.C. § 112, second paragraph rejections labeled a), b), c), d), e), g), h), i), j), k), l), m), n), o), p), q), s), t), u) and v) of the office action, which are hereby **withdrawn**.

However, with regards to the 35 U.S.C. § 112, second paragraph rejections labeled r) the applicant's amendments and remarks have been fully considered but they are not persuasive.

r) The applicants' stated that the claims as amended satisfy the requirements of the second paragraph of the statute. However, claim 12, which

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corresponds to newly added claim 24 generically claims the method of treating a disorder responsive to the activity of nAChR modulators. The rejection of claim 12 was on the grounds that it is indefinite, in that it is not known which diseases are capable of being responsive to the activity of nAChR modulators. The scope of diseases and/or disorders associated with the activity of nAChR modulators could alter over time. The applicants' are not entitled to preempt the efforts of others.

Newly added claim 24 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for reasons of record and stated above.

5. The applicant's amendments and arguments are sufficient to overcome the 35 U.S.C. § 102, anticipation rejection of claims 1-4, labeled paragraph 8) of the last office action, which is hereby **withdrawn**.

6. The applicant's amendments and arguments are sufficient to overcome the 35 U.S.C. § 102, anticipation rejection of claims 1-4, labeled paragraph 9) of the last office action, which is hereby **withdrawn**.

In view of the amendment dated October 1, 2003, the following new grounds of rejection apply:

Priority

7. An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)). The specific reference to any prior nonprovisional application must include the relationship (i.e., continuation, divisional, or continuation-in-part) between the applications except when the reference is to a prior application of a CPA assigned the same application number.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

8. Claims 17-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

- a) Claims 17-20 and 23-25 are vague and indefinite in that it is not known what is meant by "Derivative" which implies more than what is positively recited
- b) Claims 17, 18 and 23-25 are vague and indefinite in that it is not known what is meant by the definition of R which is not divalent as indicated in the moiety -R-B-R- of formula (II).
- c) Claims 17-19 and 23-25 are vague and indefinite in that it is not known what is meant by the definition of R¹ which is not divalent as indicated in the moiety -R¹-B-R¹- of formula (III).

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- d) Claims 17, 18 and 23-25 are vague and indefinite in that it is not known what is meant by the definition of R and R¹ which is not divalent as indicated in the moiety -R-B-R¹- of formula (IV).
- e) Regarding claim 17, the phrase "i.e." renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).
- f) Claims 17, 18 and 23-25 are vague and indefinite in that it is not known what is meant by the moiety "R-R-" with respect to formula (II), which is missing a point of attachment.
- g) Claims 17, 18 and 23-25 are vague and indefinite in that it is not known what is meant by "-R-" with respect to formula (II), which indicates when R is absent in only one of the two compounds making up the dimeric compound. However, there is no indication of the variable B.
- h) Claims 17, 18 and 23-25 are vague and indefinite in that it is not known what is meant by the moiety "R-B-R¹" in formula (IV), which is missing both points of attachment.
- i) Claims 17, 18 and 23-25 are vague and indefinite in that it is not known what is meant by the moiety "R-R¹-" with respect to formula (IV), which is missing a point of attachment.
- j) Claims 17, 18 and 23-25 are vague and indefinite in that it is not known what is meant by the moiety "R-B" with respect to formula (IV), which is missing both points of attachment.

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- k) Claim 17 recites the limitation "R-B" in formula (IV). There is insufficient antecedent basis for this limitation in the claim.
- l) Claims 17-19 and 23-25 are vague and indefinite in that it is not known what is meant by the moiety " R^1-R^1 -" with respect to formula (III), which is missing a point of attachment.
- m) Claims 17-19 and 23-25 are vague and indefinite in that it is not known what is meant by " $-R^1-$ " with respect to formula (III), which indicates when R^1 is absent in only one of the two compounds making up the dimeric compound. However, there is no indication of the variable B.
- n) Claims 17, 18 and 23-25 are vague and indefinite in that it is not known what is meant by the moiety " R^1-B-R " in formula (IV), which is missing both points of attachment.
- o) Claims 17, 18 and 23-25 are vague and indefinite in that it is not known what is meant by the moiety " R^1-R- " with respect to formula (IV), which is missing both points of attachment.
- p) Claims 17, 18 and 23-25 are vague and indefinite in that it is not known what is meant by the moiety " R^1-B " with respect to formula (IV), which is missing both points of attachment.
- q) Claim 17 recites the limitation " R^1-B " in formula (IV). There is insufficient antecedent basis for this limitation in the claim.
- r) Claims 17-19 and 23-25 are vague and indefinite in that it is not known what is meant by alkyl-onium salt, a dialkyl-onium salt, cycloalkyl-onium salt, an

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alkyl-cycloalkyl-onium salt, a dicycloalkyl-onium salt, an alkyl-cycloalkylalkyl-onium salt, a cycloalkyl0cycloalkyl-onium salt, or a dicycloalkylalkyl-onium salt.

- s) Claims 17-19 and 23-25 are vague and indefinite in that it is not known what is meant by the definition of ALK wherein ALK is alkyl, alkenyl or alkynyl which are mono-valent moieties, however ALK is divalent.
- t) Claim 18 recites the limitation "ethylenethio" in 6th moiety for the definition of R¹. There is insufficient antecedent basis for this limitation in the claim.
- u) Claim 18 recites the limitation "propylenethio" in 7th moiety for the definition of R¹. There is insufficient antecedent basis for this limitation in the claim.
- v) Claim 18 recites the limitation "butylenethio" in 8th moiety for the definition of R¹. There is insufficient antecedent basis for this limitation in the claim.
- w) Claim 18 recites the limitation "pentylenethio" in 9th moiety for the definition of R¹. There is insufficient antecedent basis for this limitation in the claim.
- x) Claim 18 recites the limitation "ethyleneseleno" in 10th moiety for the definition of R¹. There is insufficient antecedent basis for this limitation in the claim.
- y) Claim 18 recites the limitation "propyleneseleno" in 11th moiety for the definition of R¹. There is insufficient antecedent basis for this limitation in the claim.

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- z) Claim 18 recites the limitation "butyleneseleno" in 12th moiety for the definition of R¹. There is insufficient antecedent basis for this limitation in the claim.
- aa) Claim 18 recites the limitation "pentyleneseleno" in 13th moiety for the definition of R¹. There is insufficient antecedent basis for this limitation in the claim.
- ab) Claim 18 recites the limitation "N-2-pyrrolinyl" in 18th moiety for the definition of R¹. There is insufficient antecedent basis for this limitation in the claim.
- ac) Claim 18 recites the limitation "N-3-pyrrolinyl" in the first line of page 5 for the definition of R¹. There is insufficient antecedent basis for this limitation in the claim.
- ad) Claim 18 recites the limitation "N-(1,4,5,6-tetrahydropyridyl)" in the second line of page 5 for the definition of R¹. There is insufficient antecedent basis for this limitation in the claim.
- ae) Claim 18 recites the limitation "N-(1,4,5,6-tetrahydropyridyl)" in the third line of page 5 for the definition of R¹. There is insufficient antecedent basis for this limitation in the claim.
- af) Claim 18 recites the limitation "5-propyl-1,2-epoxy-1-oxy" in the eighth line from the bottom of page 5 for the definition of R¹. There is insufficient antecedent basis for this limitation in the claim.

ag) Claim 18 recites the limitation "5-(cyclobutylmethoxy" in the fifth line from the bottom of page 5 for the definition of R¹. There is insufficient antecedent basis for this limitation in the claim.

ah) Claim 18 is vague and indefinite in that it is not known what is meant by the definition of R¹, which is not stated as a proper Markush grouping. There is no "and" before the last species.

ai) Regarding claim 19, the phrase "i.e." renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

aj) Claim 21 recites the limitation "1-(6-bromo-5-methoxy-3-pyridyl)-homopiperazine" in the species of claim 21. There is insufficient antecedent basis for this limitation in the claim.

ak) Claim 22 recites the limitation "1-(6-bromo-5-methoxy-3-pyridyl)-homopiperazine" in the species of claim 22. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

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9. Claims 17 and 19 are rejected under 35 U.S.C. 102(a) as being anticipated by ISHIWATA et al., WO 99/42446 (U.S. equivalent 6,448,242). ISHIWATA teaches the compounds of the instant invention where R is H and $-R^1-B-R^1-$ is $-CH_2-CH_2-$, $-CH_2-CH_2-CH_2-$, or $-(CH_2)_8-$. See examples 22, 23 and 24.

10. Claims 17, 19 and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by KANEKO et al., U.S. 4,639,415. KANEKO teaches the compounds of the instant invention where R is $-(CH_2)_{11}-CH_3$ and $-R^1-B-R^1-$ is $-CH_2-$. See example E-11.

11. Claims 17, 19 and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by GREEN et al., U.S. 4,025,617. GREEN teaches the compounds of the instant invention where R is H and $-R^1-B-R^1-$ is $-CH_2-CH=CH-CH_2-$. See example 4.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brenda Coleman whose telephone number is 571-272-0665. The examiner can normally be reached on 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mukund Shah can be reached on 571-272-0674. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should

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you have questions on access to the Private PAIR system, contact the Electronic

Business Center (EBC) at 866-217-9197 (toll-free).



Brenda Coleman

Primary Examiner Art Unit 1624

August 23, 2004